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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 09/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/725,829	CHYE ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *10 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *2,4-7 and 48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 8-47 and 49-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: search results

RDD

DETAILED ACTION

1. Claims 1-58 are pending. Claims 2, 4-7 and 48 are withdrawn from consideration as being drawn to non-elected inventions.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from the Brief Description of Fig. 10b.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth herein. Failure to fully comply with both of these requirements in the time period set forth in this Office action will be held to be non-responsive.

4. The objection to claims 8, 16, 24, 27, 30, 33, 36, 39, 49, 50 for reciting nonelected SEQ ID NOs: is withdrawn in light of Applicant's amendment of the claims.

5. The objection to claims 12-15, 17-18, 20-23, 25-26, 28-29, 31-32, 34-35, 37-38, 40-45, 51-52 and 56-58 for informalities is withdrawn in light of Applicant's amendment of the claims.

6. The objection to claim 4-45 under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to claims in an alternative form is withdrawn in light of Applicant's amendment of the claims.

7. The objection to claim 23 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in light of Applicant's amendment of the claim.

8. The rejection of claims 1,3, and 49-51 under 35 U.S.C. 102(b) as being anticipated by Xu et al (Plant Molecular Biology, 2001, 47:727-738) is withdrawn as the rejection should have been a rejection under 35 U.S.C. 102(a).

9. The rejection of claims 1, 3, 24, 26, 27 and 29 under 35 U.S.C. 103(a) as being unpatentable over Daniell et al (2001, Plant Physiology, 127:13 1-141) and Solomon et al (1999, Plant Cell, 11:431-443) in view of Xu et al (2001, Plant Mol. Biol., 47:727-738) is withdrawn as the rejection is a repeat of other rejections.

Claim Rejections - 35 USC § 112

10. Claims 46-47 and 53-54 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims are drawn to plasmids pSa7 or pMLVHisP or plants comprising them, which are subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 11 March 2005. Applicant's arguments filed 10 June 2005 have been fully considered but they are not persuasive.

The claim is directed to specific plasmids. Since the plasmids are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the plasmids are not so obtainable or available, a

deposit of microorganism containing said plasmids may satisfy the requirements of 35 USC 112. The specification does not disclose a repeatable process to obtain the plasmids and it is not apparent if the plasmids are readily available to the public. Thus, a deposit is required for enablement purposes.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;
(d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and,
(e) the deposit will be replaced if it should ever become inviable.

In addition, the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.801 - 1.809 [MPEP 2401-2411.05] for additional explanation of these requirements.

Applicant urges that the construction of pSA7 is described on pg 40 and Fig 10a (response pg 15-16).

This is not found persuasive. Pg 40 says that the Gus gene of pBI121 was replaced with the SaPIN2a cDNA, but it is not clear how that was done.

Applicant details the construction of pMLVHisP , stating this was described on pg 43 and Fig. 180-19 (response pg 16).

This is not found persuasive. None of the listed polylinkers are in the specification, and none of the rest of the information is. Thus, the specification does not teach the construction of npMVLHisP.

11. Claims 3, 11-15, 19-23, 27-29, 33-35, 39-45, 50-52, and 55-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 11 March 2005. Applicant's arguments filed 10 June 2005 have been fully considered but they are not persuasive.

The claims are broadly drawn to an isolated nucleic acid molecule having a nucleotide sequence that hybridizes to SEQ ID NO:1, wherein the nucleotide sequence encodes a protein having proteinase inhibitor activity.

Applicant does not describe an isolated nucleic acid molecule having a nucleotide sequence that hybridizes to SEQ ID NO:1, wherein the nucleotide sequence encodes a protein having proteinase inhibitor activity. Applicant has not described any structural features of SEQ ID NO:1 that are essential for function and Applicant has not described if nucleic acid molecule having a nucleotide sequence that hybridizes to SEQ ID NO:1 possesses the structural features that are essential for function. Furthermore, there is no functional description of an isolated nucleic acid molecule having a nucleotide sequence that hybridizes to SEQ ID NO:1. In addition,

Applicant does not describe the sufficient structural elements of a representative number of nucleic acids that encode a proteinase inhibitor II.

Hence, Applicant has not, in fact, described an isolated nucleic acid molecule having a nucleotide sequence that hybridizes to SEQ ID NO:1 wherein the nucleotide sequence encodes a protein having proteinase inhibitor activity within the full scope of the claims, therefore the specification fails to provide an adequate written description of the claimed genus.

Therefore, given the lack of written description in the specification with regard to the structural and functional characteristics of the claimed nucleic acids, it is not clear that Applicant was in possession of the claimed genus at the time this application was filed.

Applicant urges that the structural features of SEQ ID NO:1 that are essential for function are described on pg 9, lines 1-15; SaPIN2a contains 2 inhibitory domains, one, amino acids 30-83, is inhibitory for trypsin and the other, amino acids 87-140, is inhibitory for chymotrypsin (response pg 18).

This is not found persuasive. The structure of SEQ ID NO:1 is not the issue, as the full length of the sequence is described.

Applicant urges that hybridization is well-known in the art; structure is provided in that the DNAs hybridize with SEQ ID NO:1 and function is provided in that they are proteinase inhibitors, the nucleic acid can be expressed in plants and the inhibitor activity assayed by methods well-known in the art (response pg).

This is not found persuasive. Proteinase inhibitors in plants have a broad range of specific functions, include at least fifteen families with specific structural and functional characteristics (Wilson, 1997, In: Cellular and Molecular Biology of Plant Seed Development,

Larkins et al, eds., pg 331-374; see pg 333, right column, paragraph 3), and have inhibitory activity towards different proteinases (Wilson, Table 1). The specification does not describe the specific function of proteinase inhibitors that hybridize to SEQ ID NO:1.

The genus of proteinase-inhibitor encoding nucleic acids that hybridize to SEQ ID NO:1 is very broad, and includes nucleic acids that hybridize to only a small portion of SEQ ID NO:1; thus, SEQ ID NO:1 is not sufficient to represent their sequences. The only species described in the specification are SEQ ID NO:1 and 3. These species do not describe the full scope of this very broad genus.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997) at pg 1406:

> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

12. Claims 3, 11-15, 19-23, 27-29, 33-35, 39-47 and 50-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids encoding SEQ ID NO:2, vectors and plants comprising them, and methods of using them to inhibit programmed cell death, does not reasonably provide enablement for proteinase-inhibitor encoding nucleic acids that hybridize to SEQ ID NO:1, vectors and plants comprising them, and methods of using them to inhibit programmed cell death. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as set forth in the Office action mailed 11 March 2005. Applicant's arguments filed 10 June 2005 have been fully considered but they are not persuasive.

The claims are broadly drawn to proteinase-inhibitor encoding nucleic acids that hybridize to SEQ ID NO:1, vectors and plants comprising them, and methods of using them to inhibit programmed cell death.

The instant specification, however, only provides guidance for only provide guidance for cloning and DNA sequence analysis of the 5'-end of the Sapin2b cDNA (pg 36); expression patterns of Sapin2a and Sapin2b (pg 45); localization of Sapin2a and Sapin2b mRNA and proteins in flowers (pg 45-46); immunogold labeling of Sapin2a and Sapin2b in S. americanum ovule (pg 47), generation of transgenic of lettuce with Sapin2a cDNA (pg 40 and 47); Southern blot analysis of transgenic lettuce (pg 48); expression of Sapin2a mRNA in transgenic lettuce (pg 49); trypsin and chymotrypsin inhibitory activities and endogenous trypsin- and chymotrypsin-like activity assays (pg 42 and 50); preliminary insect feeding assay with primary transgenic lettuce plants (pg 43 and 51); plasmid construction for plastid transformation of tobacco (pg 43 and 52) and screening of the plastid-transformed tobacco for integration of Sapin2a cDNA (pg 44).

The instant specification fails to provide guidance for where to find proteinase-inhibitor encoding nucleic acids that hybridize to SEQ ID NO:1.

The instant specification fails to provide guidance for which amino acids of SEQ ID NO:2 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain proteinase-inhibitor activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

Making substitutions in proteins is not a predictable art. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1)..

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate proteinase-inhibitor-encoding nucleic acids that hybridize to SEQ ID NO:1. Making all possible single amino acid substitutions in an 148 amino acid long protein like that encoded by SEQ ID NO:1 would require making and analyzing 19^{148} nucleic acids; these proteins would have 99.3% identity to SEQ ID NO:2. Because nucleic acids that hybridize to SEQ ID NO:1 would encode proteins with many amino acid substitutions, many more than 19^{148} nucleic acids would need to be made and analyzed. Guo et al (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid changes, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2). Thus, making and analyzing proteinase-inhibitor encoding nucleic acids that hybridize to SEQ ID NO:1 would require undue experimentation.

As the specification does not describe the transformation of any plant with a proteinase-inhibitor encoding nucleic acids that hybridize to SEQ ID NO:1 other than SEQ ID NOs:1 and 3, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with inhibited cell death, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

Applicant urges that nucleic acid that hybridize to SEQ ID NO:1 can be found by screening libraries, citing Sambrook, or by use of degenerate primers and PCR, as described in sections 5.1 and 5.3-5.8 of the specification; such methods are well-known in the art and are not undue experimentation (response pg 20-21).

This is not found persuasive. The specification does not teach in which organisms such nucleic acids would be found. Thus, screening libraries from all plant species in order to find nucleic acids that hybridize to SEQ ID NO:1 would be undue experimentation. Sambrook could not be considered because it was not sent.

Applicant urges that making amino acid substitutions is not necessary because all that is required is screening libraries (response pg 21-22).

This is not found persuasive. The claims are not limited to nucleic acids isolated from plant species, but include man-made nucleic acid sequences. Thus, the specification must teach how to make these nucleic acids; it does not.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claim 1, 3 and 49-51 are rejected under 35 U.S.C. 102(a) as being anticipated by Xu et al (Plant Molecular Biology, 2001, 47:727-738).

Xu et al teach a nucleotide sequence comprising SEQ ID NO:1 (see search results sent with the action mailed 11 March 2005) and said sequence cloned in a vector having regulatory elements (page 729, column 1, paragraph 2).

15. Claim 3, 11-12, 19-20, 33-34, 39-40, 49-51, 55 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Anderson et al (29 February 2000, U.S. Patent 6,031,087). The rejection is repeated for the reasons of record as set forth in the Office action mailed 11 March 2005. Applicant's arguments filed 10 June 2005

Anderson et al disclosed a nucleotide sequence that hybridizes to SEQ ID NO: 1 because it has 67.3% similarity to it (see search results sent with the action mailed 11 March 2005). Anderson et al disclosed a method of increasing or enhancing resistance of a plant to insect or other pathogen infestation, said method comprising introducing a nucleic acid molecule into cell or group of cells of said plant, regenerating a plant therefore and growing said plant for a time and under conditions sufficient to permit expression of said nucleic acid into a proteinase inhibitor or precursor thereof which inhibits growth and infestation by said pathogen (column 38,

claim 7), a recombinant vector comprising a polynucleotide that comprises a nucleotide sequence that hybridizes to the nucleotide sequence of SEQ ID NO:1 (column 20, line 45), and cells infected with a recombinant virus containing the recombinant vector comprising a polynucleotide that comprises a nucleotide sequence that hybridizes to of SEQ ID NO:1 (column 20, line 55). Programmed cell death would be inherent in a method having the same steps. have been fully considered but they are not persuasive.

Applicant urges that there is no evidence that the sequence of Anderson would hybridize to SEQ ID NO:1 (response pg 23).

This is not found persuasive because there are long stretches of the Anderson sequence that have much higher than 67.3% identity; these would hybridize to SEQ ID NO:1 under the recited conditions.

16. Claims 3, 50 and 55 are rejected under 35 U.S.C. 102(b) as being anticipated by Alcala et al (2001, GenBank Accession No. AW035333).

Alcala et al teach a proteinase-inhibitor encoding nucleic acid that would hybridize to SEQ ID NO:1 because it has 79.4% identity to it and has long stretches of even higher identity (see search results). The nucleic acid is in a vector because it was isolated from a library, and the vector would inherently be in a recombinant cell.

17. Claims 3, 11-12, 14-15, 19-20, 22-23, 27-28, 33-34, 39-40, 42, 50-52 and 55-58 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al (1989, Proc. Natl. Acad. Sci. USA 86:9871-9875) taken with the evidence of Graham et al (1985, J. Biol. Chem. 260:6561-6564).

Johnson et al teach tobacco plants nuclearly transformed with vectors comprising a 35S promoter operatively linked to the TI-II nucleic acid and methods of producing the protein in and isolating from the plants (pg 9872, right column, paragraphs 2-3; Fig. 1-2); these methods would inherently be ones of inhibiting programmed cell death in the plant, and would inherently inhibit an endogenous trypsin- or chymotrypsin-like proteinase activity in the plant. Tobacco would be a "leafy vegetable".

Graham et al teach the TI-II nucleic acid, which is a proteinase-inhibitor encoding nucleic acid that would hybridize to SEQ ID NO:1 because it has a 35 nucleotide long stretch of 100% identity (see search results). The DNA was in a vector, which was in a recombinant host cell (pg 6561, right column, paragraphs 6-7).

Claim Rejections - 35 USC § 103

18. Claims 1, 3, 8-9, 11-12, 14-17, 19-20, 30-31, 33-34, 36-37, 39-40, 42, 49-52 and 55-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al (PNAS, 86:9871-9875, 1989) in view of Xu et al (2001, Plant Mol. Biol., 47:727-738). The rejection is modified from the rejection set forth in the Office action mailed 11 March 2005. Applicant's arguments filed 10 June 2005 have been fully considered but they are not persuasive.

Johnson et al disclosed plant transformation plasmids containing either proteinase inhibitor I or II coding regions, under the control of the CaMV 35S promoter (page 9872, column 2, second paragraph). Plants were transformed with these plasmids by nuclear transformation. The leaf extracts from tobacco plants transformed with the plasmids were analyzed for the expression of the proteins by assaying for the ability of the proteins to inhibit trypsin and

chymotrypsin (page 9871, column 2, sixth paragraph; page 9872, column 2, third paragraph). Johnson et al do not teach a nucleic acid of SEQ ID NO:1.

The teachings of Xu et al are discussed above.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method for producing a transformed plant and selecting a transformed plant in which said nucleotide sequence is expressed as described by Johnson et al to substitute a recombinant vector comprising a polynucleotide that comprises the nucleotide SEQ ID NO: 1 or an isolated nucleic acid molecule having a nucleotide sequence that hybridizes to a proteinase inhibitor 11 nucleotide sequence of SEQ ID NO:1. One of ordinary skill in the art would have beçn motivated to do so because expression of plant defense proteins in plants can enhance pest/pathogen protection in transgenic crops (Xu et al, pg 728, column 1, paragraph 2). Thus, the claimed invention would have been prima facie obvious as a whole to one of ordinary skill in the art, at the time it was made, especially in the absence of evidence to the contrary.

Applicant urges that Xu is not a proper prior art reference (response pg 24).

This is not found persuasive; Xu is a prior art reference under 102(a) as it was written by a different inventive entity.

19. Claims 1, 3, 8, 10-11, 13, 16, 18, 19, 21, 30, 32-33, 35-36, 38-39, 41, 49-52, 55 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu et al (2001, Plant Mol. Biol., 47:727-738) in view of Daniell et al (U.S. Patent Application Publication No: 2004/0210966; effective filing date February 2001) and further in view of Zhang et al (Plant Physiology, 127:131-141, 2001, abstract). The rejection is modified from the rejection set forth in the Office

action mailed 11 March 2005. Applicant's arguments filed 10 June 2005 have been fully considered but they are not persuasive.

Daniell et al disclosed method for producing a transformed plant with several genes into a single T-DNA. These genes are insecticidal toxin genes such as Bacillus thuringiensis genes, protease inhibitors, the cowpea trypsin inhibitors, and the potato proteinase inhibitor II via plastid transformation (paragraphs 23-31 and 116, claims 1, 5) and said transgenic plants produced the proteins as measured by ELISA and insect bioassays (paragraphs 131-132; claim 15). Daniell et al do not plants transformed with SEQ ID NO:1.

The teachings of Xu et al are discussed above.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of transforming a chloroplast as taught by Daniell et al to substitute a recombinant vector comprising a polynucleotide comprising SEQ ID NO: 1 as taught by Xu et al. One of ordinary skill in the art would have been motivated to do so because very high and uniform levels of gene expression can be observed in different transplastomic lines, probably due to the identical insertion sites, in contrast to nuclear transformation where random insertion occur (Zhang et al, abstract). In addition, Daniell et al taught that plants transformed by plastid transformation showed the highest level of expression (paragraph 8).

Applicant urges that Xu is not a proper prior art reference (response pg 24).

This is not found persuasive; Xu is a prior art reference under 102(a) as it was written by a different inventive entity.

20. Claims 1, 3, 16, 17, 19, 20, 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Solomon et al (1999, Plant Cell, 1 1:431-443) in view of Xu et al (2001, Plant

Mol. Biol., 47:727-738). The rejection is repeated for the reasons of record as set forth in the Office action mailed 11 March 2005. Applicant's arguments filed 10 June 2005 have been fully considered but they are not persuasive.

Solomon et al disclosed transformation of soybean suspension-cultured cells with a plasmid containing either a soybean cystatin (cysteine proteinase inhibitor), or Kunitz, (inhibitor of the trypsin-like proteases), or a Bowman-Birk-type inhibitor (a chymotrypsin and elastase inhibitor) operably linked to the 355 promoter. Ectopic expression of cystatin blocked programmed cell death triggered by an avirulent strain Pseudomonas syringae pv glycinea (pg 435, column 2, paragraph 1) or by oxidative stress (pg 435, column 1, paragraph 4). Solomon et al do not teach a method for inhibiting programmed cell death and senescence in a transformed plant or plant part comprising transforming a plant with a recombinant vector comprising a SEQ ID NO:1 and selecting a transformed plant in which said polynucleotide is expressed.

The teachings of Xu et al are discussed above.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method for inhibiting programmed cell death and senescence in a transformed plant or plant part as taught by Solomon et al to substitute SEQ ID NO:1 as described by Xu et al. One of ordinary skill in the art would have been motivated to do so because in order to analyze the role of specific proteases in programmed cell death. One of ordinary skill in the art would have been motivated to do so because in order to inhibit programmed cell death in plants.

Applicant urges that Xu is not a proper prior art reference (response pg 24).

This is not found persuasive; Xu is a prior art reference under 102(a) as it was written by a different inventive entity.

21. Claims 1, 3, 24, 25, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urwin et al (1998, Planta, 204: 472-479) in view of Xu et al (2001, Plant Mol. Biol., 47:727-738). The rejection is repeated for the reasons of record as set forth in the Office action mailed 11 March 2005. Applicant's arguments filed 10 June 2005 have been fully considered but they are not persuasive.

Urwin et al disclosed a recombinant fusion protein expression in E. coli and analysis of inhibitory activity. The oryzacystatin (cysteine inhibitor) and cowpea trypsin inhibitor were joined as translational fusions, expressed in E. coli and the expressed protein were purified using the 6-His-tag. After the removal of the His tag peptide from the fusion protein, the protein was analyzed for its ability to inhibit the activity of papain and trypsin (pg 474, column 1, paragraph 3). Urwin et al also disclosed a transformed plants transformed with a plasmid containing oryzacystatin (cysteine inhibitor) and cowpea trypsin inhibitor genes in a single TDNA by nuclear transformation. Urwin et al do not teach a transformed plants comprising SEQ ID NO:1.

The teachings of Xu et al are discussed above.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method for producing a heterologous protein in a plant described by Urwin et al to substitute a recombinant vector comprising a polynucleotide of SEQ ID NO: 1 or that hybridizes to SEQ ID NO: 1. One of ordinary skill in the art would have been motivated to do so because stacking or pyramiding transgenes enhanced efficacy and durability and thereby

broadening the potential of the transgenic approach (Urwin et al, pg 473, column 1, paragraph 3).

22. Claims 43-47 and 53-54 are free of prior art.

Conclusion

23. No claim is allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached at (571) 272-0745.

The central fax number for official correspondence is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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August 26, 2005

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